



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,888	02/10/2004	Rainer Endermann	Le A 36 499	1423
35969	7590	08/04/2009	EXAMINER	
Barbara A. Shimei			WANG, SHENGJUN	
Director, Patents & Licensing			ART UNIT	PAPER NUMBER
Bayer HealthCare LLC - Pharmaceuticals				1617
555 White Plains Road, Third Floor				
Tarrytown, NY 10591				
MAIL DATE		DELIVERY MODE		
08/04/2009		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/775,888	ENDERMANN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 26 May 2009.  
 2a) This action is **FINAL**.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-3 and 6-14 is/are pending in the application.  
 4a) Of the above claim(s) 6-8 is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) \_\_\_\_\_ is/are rejected.  
 7) Claim(s) 1-3 and 9-14 is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____ .
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date _____.	6) <input type="checkbox"/> Other: _____ .

## **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on May 26, 2009 has been entered.

### ***Claim Rejections 35 U.S.C. 112***

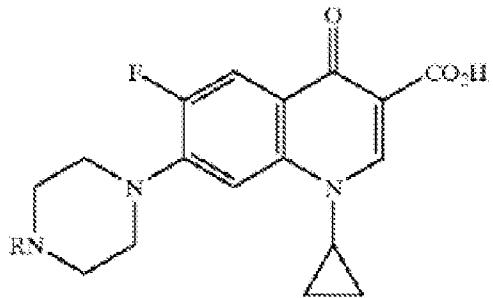
1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-3 and 9-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

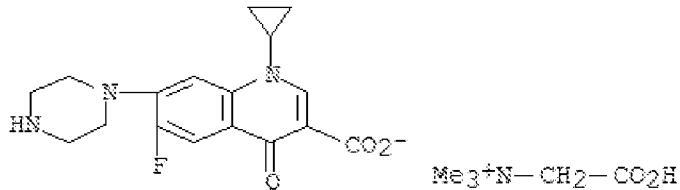
3. The term "slightly soluble" in claim 1 is a relative term which renders the claim indefinite. The term "slightly soluble" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claims 1-3 are indefinite as to the "slightly soluble salt" encompassed thereby.

4. Claim 1 and 14 recite "solid betaine" of the formula (III)



. It is unclear if the claim define the formula (III) as (solid)

betaine, or it means a betaine salt of formula (III). Note, art acceptable formula for betaine salts, such as ciprofloxacin betaine is as following:



The claims are indefinite as to the compounds encompassed by the “solid betaine of the formula (III).

***Claim Rejections 35 U.S.C. 102***

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Because of the ambiguity of the claims (see the rejection above), the claims are interpreted broadly to encompass both the compound represented by formula (III) its betaine salts.

7. Claims 1, 2 and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Pikiewicz et al. (US 2004/0009126 A1).

8. Pikiewicz et al. teach a method of treating bacterial lung infection comprising locally administration of ciprofloxacin by inhalation, wherein the ciprofloxacin is in the form of particle and may be in the form of dry powder. See, particularly, the abstract, paragraphs [0064] and [0069], and the claims.

***Claim Rejections 35 U.S.C. 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 1, 2 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayer et al. in view of Li et al.

Mayer et al. treated anthrax lung infection by administering to the patients ciprofloxacin. The administration is carried out intravenously. See, particularly, the abstract, pages 2550 and 2551. Mayer et al. further disclosed that it is well known that ciprofloxacin is effective against anthrax and is a standard treatment of anthrax. See, page 252, the right column.

Mayer et al. do not teach expressly local administration as herein claimed.

However, Li et al. teach ciprofloxacin administration intravenously or orally have relatively unfavorable pharmacokinetic profile in the lower respiratory track. Li also disclosed that Aerosol inhalation as means of drug delivery to the respiratory tract has been well established in the treatment of lung disease, and dry powder inhaler have received increasing

attention in the art. Li et al. further teaches a ciprofloxacin loaded particles for dry powder inhaler delivery to the respiratory track by inhalation. See, particularly, the abstract and introduction at page 825.

Therefore, it would have been *prima facie* obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to use dry powder inhaler for delivery ciprofloxacin composition, such as those disclosed by Li, directly to respiratory track for treatment of respiratory track bacterial infection, such as anthrax infection.

A person of ordinary skill in the art would have been motivated to use dry powder inhaler for delivery ciprofloxacin composition, such as those disclosed by Li, directly to respiratory track for treatment of respiratory track bacterial infection, such as anthrax infection because the delivery method is more effective than intravenous or oral delivery.

11. Claims 3, 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayer et al. in view of Li et al. for reasons set forth above, and further in view of Grohe et al. (US 4,670,444, IDS), and Vetter et al. (US 5,808,076).

12. Mayer and Li as whole do not teach expressly the embonate salts of ciprofloxacin.

13. However, Grohe et al. disclose ciprofloxacin or its acid additional salts are similarly useful as antibacterial agents against a wider spectrum of gram positive and gram-negative bacteria. See, columns 10-11 and the claims. Vetter et al. teaches that incorporating embonic acid with ciprofloxacin or enrofloxacin with mask the bitterness of ciprofloxancin and enrofloxacin. See, particularly, the claims.

14. Therefore, it would have been *prima facie* obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to make a acid added ciprofloxacin salt with embonic acid and use it for dry powder inhalation delivery.

15. A person of ordinary skill in the art would have been motivated to make a acid added ciprofloxacin salt with embonic acid and use it for dry powder inhalation delivery because it is known acid additive salts of ciprofloxacin are known to be similarly useful as ciprofloxacin and embonic acid is particularly known to provide benefit for masking the bitterness of ciprofloxacin. Further, making an acid addition salt of an organic compound is within the purview of skilled artisan.

16. Claims 1, 2 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pikiewicz et al. (US 2004/0009126 A1) in view of Kanikanti et al. (WO 02/00219 A1, US 2004/0024018 A1 is a English equivalence).

17. Pikiewicz et al. teach a method of treating bacterial lung infection comprising locally administration of ciprofloxacin by inhalation, wherein the ciprofloxacin or its salt, is in the form of particle and may be in the form of dry powder. See, particularly, the abstract, paragraphs [0064] and [0069], and the claims.

18. Pikiewicz et al. do not teach expressly the employment of the particular salt, ciprofloxacin betaine.

19. However, Kanikanti et al. teaches that ciprofloxacin betaine is a known salt of ciprofloxacin useful for therapeutical purpose. See, particularly, paragraphs [0039]-[0047].

20. Therefore, it would have been obvious to use ciprofloxacin betaine as a ciprofloxacin salt in Pikiewicz's method.

21. A person of ordinary skill in the art would have been motivated to use ciprofloxacin betaine as a ciprofloxacin salt in Pikiewicz's method because ciprofloxacin betaine is one of few known salt of ciprofloxacin. Furthermore, as stated in KSR vs. Teleflex, where the court states: "When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. **If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.** In that instance the fact that a combination was obvious to try might show it was obvious under section 103." In the instant case, it would have been obvious to try the known salts of ciprofloxacins for an optimal therapeutical result. Since there are not many known ciprofloxacin salts.

22. Claims 1, 2 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayer et al. in view of Li et al. and Kanikanti et al. (WO 02/00219 A1, US 2004/0024018 A1 is a English equivalence).

Mayer et al. treated anthrax lung infection by administering to the patients ciprofloxacin. The administration is carried out intravenously. See, particularly, the abstract, pages 2550 and 2551. Mayer et al. further disclosed that it is well known that ciprofloxacin is effective against anthrax and is a standard treatment of anthrax. See, page 252, the right column.

Mayer et al. do not teach expressly local administration as herein claimed or the employment of ciprofloxacin betaine.

23. However, Li et al. teach ciprofloxacin administration intravenously or orally have relatively unfavorable pharmacokinetic profile in the lower respiratory track. Li also disclosed that Aerosol inhalation as means of drug delivery to the respiratory tract has been well

established in the treatment of lung disease, and dry powder inhaler have received increasing attention in the art. Li et al. further teaches a ciprofloxacin loaded particles for dry powder inhaler delivery to the respiratory track by inhalation. See, particularly, the abstract and introduction at page 825. Kanikanti et al. teaches that ciprofloxacin betaine is a known salt of ciprofloxacin useful for therapeutical purpose. See, particularly, paragraphs [0039]-[0047].

Therefore, it would have been *prima facie* obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to use dry powder inhaler for delivery ciprofloxacin composition, such as ciprofloxacin betaine, directly to respiratory track for treatment of respiratory track bacterial infection, such as anthrax infection.

A person of ordinary skill in the art would have been motivated to use dry powder inhaler for delivery ciprofloxacin composition, such as such as ciprofloxacin betaine, directly to respiratory track for treatment of respiratory track bacterial infection, such as anthrax infection because the delivery method is more effective than intravenous or oral delivery, and ciprofloxacin betaine is a known salt of ciprofloxacin useful for therapeutical purpose.

24. Claims 3, 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayer et al. in view of Li et al. Kanikanti et al. (WO 02/00219 A1, US 2004/0024018 A1 is a English equivalence), for reasons set forth above, and further in view of Grohe et al. (US 4,670,444, IDS), and Vetter et al. (US 5,808,076).

25. Mayer and Li as whole do not teach expressly the embonate salts of ciprofloxacin, or ciprofloxacin.

26. However, Grohe et al. disclose ciprofloxacin or its acid additional salts are similarly useful as antibacterial agents against a wider spectrum of gram positive and gram-negative bacteria. See, columns 10-11 and the claims. Vetter et al. teaches that incorporating embonic acid with ciprofloxacin or enrofloxacin with mask the bitterness of ciprofloxancin and enrofloxacin. See, particularly, the claims.

27. Therefore, it would have been *prima facie* obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to make a acid added ciprofloxacin salt with embonic acid and use it for dry powder inhalation delivery.

28. A person of ordinary skill in the art would have been motivated to make a acid added ciprofloxacin salt with embonic acid and use it for dry powder inhalation delivery because it is known acid additive salts of ciprofloxacin are known to be similarly useful as ciprofloxacin and embonic acid is particularly known to provide benefit for masking the bitterness of ciprofloxacin. Further, making an acid addition salt of an organic compound is within the purview of skilled artisan.

#### *Response to the Arguments*

Applicants' amendments and remarks submitted January 24, 2009 have been entered and fully considered, but are found not persuasive to put the application in condition for allowance.

29. As to the arguments that cited references do not teach, either expressly or inherently the limitation of "solid betaine," the examiner maintains that the claims are interpreted broadly to encompass the compound represented by the formula (III). Applicants' attention is also directed to the new ground rejections presented in this office action.

30. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., betaine salt) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

31. Applicants also argue that Pilkiewicz reference is not a qualified prior art because the reference is not enabled for the claimed invention herein because Pilkiewicz does not specifically teach, suggest or even recognized the specific advantage envisioned by applicants. The arguments are untenable. The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

32. As to the rejection over Mayer and Li, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Particularly, it is known in the art to treat anthrax lung infection by administering to the patients ciprofloxacin. It is also known that direct delivery of ciprofloxacin to lung by inhalation of powder formulation of ciprofloxacin is a preferred method for administration. Therefore, considered the cited references as a whole, the claimed method would have been obvious.

33. Applicants' arguments about "long felt need" are unpersuasive. Establishing long-felt need requires objective evidence that an art recognized problem existed in the art for a long

period of time without solution. The relevance of long-felt need and the failure of others to the issue of obviousness depends on several factors. The alleged benefit alone cannot be sufficient to establish long-felt need. See, MPEP 716.04 for more details requirements for long-felt need.

34. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shengjun Wang/  
Primary Examiner, Art Unit 1617